Literature review

Performance of factor IX extended half-life product measurements in external quality control assessment programs

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Piet Meijer, ECAT, The Netherlands

Patients with haemophilia B are increasingly treated with extended half-life (EHL) factor IX (FIX) concentrates. The introduction of these EHL concentrates presents a major challenge for the laboratory. To understand the variation in FIX activity levels, all available diagnostic assays need to be directly compared. Therefore, in 2018 the ECAT Foundation, together with the NEQAS Blood Coagulation (United Kingdom) and RCPA (Australia), conducted a global survey to evaluate the quality of FIX measurements using FIX-deficient plasma samples spiked with recombinant FIX (rFIX), rFIXFP, rFIXFc, and N9-GP to levels at typical FIX trough (6 IU/dL) and peak levels (60 IU/dL). The manufacturer of each concentrate provided the assayed potency of the vial of concentrate used to construct samples. This was used to calculate what concentrate dilution was required to create samples containing 60 IU/dl and 6 IU/dl based on the assayed potency.

In totally 8 samples were included. Participants were asked to use their routine protocols, using one-stage assays (OSA) or chromogenic assays (CA). A summary of the results is given below.

In samples spiked with 6 IU/dL product, median (25%-75% range) FIX activity levels (OSA), were 8.0 IU/dL (7.0-9.2) for rFIX, 6.0 IU/dL (4.0-7.1) for rFIXFP, 6.6 IU/dL (5.5-8.0) for rFIXFc, and 4.9 IU/dL (3.5-8.4) for N9-GP. In samples spiked with 60 IU/dL, FIX activity levels measured (using OSA) was 63.0 IU/dL (59.9-67.0) for rFIX, 42.5 IU/dL (28.2-47.0) for rFIXFP, 50.0 IU/dL (45.0-55.0) for rFIXFc, and 34.0 IU/dL (24.8-67.5) for N9-GP. Considerable differences were observed between reagents for all samples. With CA, there was also quite some variation, but no differences between reagents.

It can be concluded that a large variation can be observed in the measurement of FIX activity levels after the administration of rFIX and EHL FIX products. Most silica-based assays show especially high levels for N9-GP. It is essential to standardise and improve the reliability of measurements of these concentrates as diagnosis and treatment monitoring are based on these results.

This study is now published in the Journal of Thrombosis and Haemostasis. This open-access publication can be reached using the following link: https://onlinelibrary.wiley.com/doi/full/10.1111/jth.14847